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09/862,417	05/23/2001	Xiao Bing Wang	TRIM4	8468

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/862,417	Wang
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 12, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 6, 9, and 11-47* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6, 9, and 11-47* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *0503*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claims 5, 7, 8 and 10 have been canceled without prejudice towards further prosecution. Claims 1-4, 6, 9, 11-14, 18-19, 22, 24-28, 31-34, and 36-38 have been amended. New claims 41-47 have been added.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1-4, 6, 9, and 11-15, 18, 20-24, 42, 45, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Okada et al. (U.S. Patent 5,521,296) (May 28, 1996).

Okada et al teach a method for detecting or quantifying a target nucleic acid in a sample (Abstract) comprising:

a) preparing at least one primer specifically matched to a predetermined position of the target nucleic acid (Example 3, Column 12, lines 24-25);

b) annealing the at least one primer from a) with the target nucleic acid to obtain a primer-nucleic acid duplex at the predetermined position of the target nucleic acid (Column 12, lines 24-38);

c) mixing the primer-nucleic acid duplex from b) with a non-terminator nucleotide, wherein at least one of four required types of nucleotides for continuous extension during primer extension reaction is omitted from the non-terminator nucleotide mixture, and wherein at least one non-terminator nucleotide is labeled with a detectable marker (Column 12, lines 35-46);:

d) performing isometric primer extension by enzymatic or chemical reaction in an appropriate buffer to form isometric primer extension products, wherein the primer extension terminates at a target nucleic acid nucleotide complementary to the omitted non-terminator nucleotide of c) (Column 12, lines 44-46); and

e) inherently detecting or quantifying the amount of labeling signal on the isometric primer extension products (Column 12, line 46). This inherency is deduced from the fact that the reaction mixture of Okada et al is exactly the same as used by the claimed invention. As okada et al teaches, "This reaction mixture was used as a probe" (Column 12, line 46), the labeling signal on the extension products made naturally in the reaction mixture is detected or quantified at a later stage. If it is not detected or quantified, it is not possible to use it as a probe.

Okada et al teach a method, wherein at least one primer is selected from a nucleic acid primer (Example 3, Column 12, lines 24-25).

Okada et al teach a method, wherein the target nucleic acid and the non-terminator nucleotide is selected from deoxyribonucleic acid (Column 11, lines 40-41).

Okada et al teach a method, wherein the non-terminator nucleotide mixture comprises: dATP, dGTP, dTTP (Column 12, lines 35-46).

Okada et al teach a method, wherein at least one non-terminator nucleotide is labeled with a detectable radioactive isotope marker (Column 12, line 43).

Okada et al teach a method, wherein the primer extension products are formed using a template-dependent enzyme DNA polymerase or a klenow fragment (Column 12, line 44).

Okada et al teach a method, wherein the target nucleic acid is synthesized enzymatically in vitro by polymerase chain reaction (Column 11, lines 7-55).

Okada et al teach a method, wherein the organism is a vertebrate or invertebrate (Examples 3-4).

Okada et al teach a method, wherein the organism is a mammal (Example 4).

Okada et al teach a method, wherein the organism is a human being (Example 4).

Okada et al teach a method, wherein an amplification step is performed on the target nucleic acid (Column 12, lines 38-46).

Okada et al teach a method, wherein the amplification step comprises polymerase chain reaction (Column 12, lines 44-46).

Okada et al teach a method, wherein the target nucleic acid is synthesized non-enzymatically (Column 5, lines 9-18).

Okada et al teach a method, wherein the non-terminator nucleotides are selected from modified deoxyribonucleotides (Column 12, line 43, radioactive P 32 labeled CTP in this case).

5. Claim 43 is rejected under 35 U.S.C. 102(b) as being anticipated by Fahy et al. (Nucleic Acids Research, (1997), Vol. 25 (15), pages 3102-3109).

Fahy et al teaches a method to detect or quantify at least one nucleic acid in a sample, the method (Abstract)comprising the steps of:

a) annealing a detectably labeled primer to a target nucleic acid (Abstract and MATERIALS AND METHODS Section, Table 2 and PCR of target DNA subsection);

b) extending the labeled primer to form isometric primer extension products by omitting at least one of four required types of nucleotides for continuous extension during primer extension reactions (MATERIALS AND METHODS Section, Primer extension assay subsection and Figure 3); and

c) detecting the labeled extension products (MATERIALS AND METHODS Section, Primer extension assay subsection, last paragraph, and Figure 3).

6. (e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

7. Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al. (U.S. Patent 6,221,592 B1) (April 24, 2001).

Schwartz et al teaches a method to detect or quantify at least one nucleic acid in a sample, the method (Abstract) comprising the steps of:

a) annealing a primer to a target nucleic acid (Figure 3, step 1);

b) extending the primer to form isometric primer extension products incorporating at least one fluorescently labeled nucleotide by omitting at least one of four required types of nucleotides for continuous extension during primer extension reactions (Figure 3, step 2); and

c) assaying for incorporation of the fluorescently labeled nucleotide within the isometric extension products (Figure 3, step 3 and Figure 4).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 16- 17 are rejected under 35 U.S.C. 103(a) over Okada et al. (U.S. Patent 5,521,296) (May 28, 1996) in view of Mizusawa et al. (Nucleic Acids Research, (1986), Vol. 14(3), pages 1319-1324).

Okada et al teach the method of claims 1-4, 6, 9, 11-15, 18, 20-24, 42, 45, and 47 as described above.

Okada et al do not teach the method, wherein the non-natural nucleotide analogs comprise 7-deaza-2'-deoxyguanosine.

Mizusawa et al. teach the method, wherein the non-natural nucleotide analogs comprise 7-deaza-2'-deoxyguanosine (Abstract and MATERIALS AND METHODS Section and Figures 1-2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method, wherein the non-natural nucleotide analogs comprise 7-deaza-2'-deoxyguanosine of Mizusawa et al. in the method of Okada et al., since Mizusawa et al. states, "Thus we conclude that the dideoxy chain termination procedure is improved by use of dC7GTP instead of dGTP because compression of bands is greatly reduced (Page 1323, last sentence) ". An ordinary practitioner would have been motivated to substitute and combine the method, wherein the non-natural nucleotide analogs comprise 7-deaza-2'-deoxyguanosine of Mizusawa et al. in the method of Okada et al., in order to achieve the express advantages , as noted by Mizusawa et al., of a revised methodology, which provides the improvement of the chain termination procedure by use of dC7GTP instead of dGTP because compression of bands is greatly reduced.

10. Claims 19, 25-40, 44 and 46 are rejected under 35 U.S.C. 103(a) over Okada et al. (U.S. Patent 5,521,296) (May 28, 1996) in view of Monforte et al. (U.S. Patent 5,965,363) (October 12, 1999)

Okada et al teach the method of claims 1-4, 6, 9, and 11-15, 18, 20-24, 42, 45, and 47 as described above.

Okada et al do not teach the method, wherein the organism is a plant, microorganism, bacteria, virus.

Monforte et al teach a method, wherein the organism is a plant, microorganism, bacteria, virus (Example 1 teaches that target nucleic acid can be any sequence, Column 24, lines 3-7).

Okada et al do not teach the method, wherein the primer comprises one or more moieties that permit affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest.

Monforte et al teach a method, wherein the primer comprises one or more moieties that permit affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest (Figures 3-12 and Examples 3, 5-7).

Okada et al do not teach the method, wherein the primer is reversibly immobilized onto a solid support to produce an immobilized target nucleic acid sequence

Monforte et al teach a method, wherein the primer is reversibly immobilized onto a solid support to produce an immobilized target nucleic acid sequence (Figures 7-8).

Okada et al do not teach the method, wherein the moieties comprises a special chemical group such as biotin.

Monforte et al teach a method, wherein the moieties comprises a special chemical group such as biotin (Examples 3 and 5 and Figures 3-12).

Okada et al do not teach the method, wherein the at least one moiety comprises a nucleotide sequence that allows the primer to link to a solid support, the solid support having a complementary sequence to the nucleotide sequence of the at least one moiety, wherein the primer is linked to the solid support via base pairing to the complementary sequence present in the solid support.

Monforte et al teach a method, wherein the at least one moiety comprises a nucleotide sequence that allows the primer to link to a solid support, the solid support having a complementary sequence to the nucleotide sequence of the at least one moiety, wherein the primer is linked to the solid support via base pairing to the complementary sequence present in the solid support (Examples 3 and 5).

Okada et al do not teach the method, wherein the primer is directly synthesized on a solid support to produce an immobilized primer sequence.

Monforte et al teach a method, wherein the primer is directly synthesized on a solid support to produce an immobilized primer sequence (Examples 3 and 5).

Okada et al do not teach the method, wherein the synthesis is accomplished by enzymatic or chemical or physical method.

Monforte et al teach a method, wherein the synthesis is accomplished by enzymatic or chemical or physical method (Examples 3 and 5).

Okada et al do not teach the method, wherein the primer and target nucleic acid is immobilized onto a solid support to produce immobilized isometric primer extension product.

Monforte et al teach a method, wherein the primer and target nucleic acid is reversibly immobilized via a photocleavable bond onto a solid support to produce an immobilized target nucleic acid sequence and isometric primer extension product (Figures 7-8).

Okada et al do not teach the method, wherein the primer can be cleaved from the solid support by a chemical, enzymatic or physical process.

Monforte et al teach a method, wherein the primer and the target nucleic acid can be cleaved from the solid support by a chemical, enzymatic or physical process (Figures 6-8, and 12 and Examples 3 and 5 and Figures 5-12 and Examples 5-6).

Okada et al do not teach the method, wherein the solid support is selected from the group consisting of beads, flat surfaces, chips, capillaries, pins or wafers.

Monforte et al teach a method, wherein the solid support is selected from the group consisting of beads, flat surfaces, chips, capillaries, pins or wafers (Column 16, lines 8-15).

Okada et al do not teach the method, wherein the immobilization is accomplished by hybridization between a complementary capture nucleic acid molecule, which has been previously immobilized to a solid support, and a portion of the nucleic acid molecule, which is distinct from the target nucleic acid sequence.

Monforte et al teach the method, wherein the immobilization is accomplished by hybridization between a complementary capture nucleic acid molecule, which has been previously immobilized to a solid support, and a portion of the nucleic acid molecule, which is distinct from the target nucleic acid sequence (Column 15, lines 27-35 and Figures 7-8, 10 and Examples 5-6).

Okada et al do not teach the method, wherein the immobilization is accomplished via direct bonding between the solid support and a portion of the nucleic acid molecule, which is distinct from the target nucleic acid sequence.

Monforte et al teach a method, wherein the immobilization is accomplished via direct bonding between the solid support and a portion of the nucleic acid molecule, which is distinct from the target nucleic acid sequence (Figure 10).

Okada et al do not teach the method, wherein the amount of labeled primer extension products are detected or quantitated by mass spectrometry.

Monforte et al teach a method, wherein the amount of labeled primer extension products are detected or quantitated by mass spectrometry (Abstract and Figures 1-15).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method, wherein the amount of labeled primer extension products are detected or quantitated by mass spectrometry of Monforte et al. in the method of Okada et al., since Monforte et al. states, "This invention relates to methods for screening nucleic acids for polymorphisms by analyzing amplified target nucleic acids using mass spectrometric techniques and to procedures for improving mass resolution and mass accuracy of these methods of detecting polymorphisms (Abstract) ". An ordinary practitioner would have been motivated to substitute and combine the method, wherein the amount of labeled primer extension products are detected or quantitated by mass spectrometry of Monforte et al. in the method of Okada et al., in order to achieve the express advantages , as noted by Monforte et al.,

of an invention which relates to methods for screening nucleic acids for polymorphisms by analyzing amplified target nucleic acids using mass spectrometric techniques and to procedures for improving mass resolution and mass accuracy of these methods of detecting polymorphisms.

Response to Amendment

11. In response to amendment, previous objection to claim 38, 112 (second paragraph) rejection, 102(b) and 103(a) rejections are hereby withdrawn. However, new 102(b) rejections and 103(a) rejections are hereby included.

Response to Arguments

12. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until

after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703)746-4979.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Arun Chakrabarti,

Patent Examiner,

June 26, 2003